

REMARKS

Status of the Claims.

Claims 1-12, and 14 are pending with entry of this amendment, claims 13, and 15-61 being cancelled and no claims being added herein. Claims 1, 2, 4-11, 12, and 14 are amended herein. These amendments introduce no new matter. Support is replete throughout the specification (*e.g.*, at page 10, paragraph 43, in the claims as originally filed, in the summary of the invention, *etc.*).

Election/Restriction.

Pursuant to a restriction requirement made final, Applicants cancel claims 15-61 with entry of this amendment. Please note, however, that Applicants reserve the right to file subsequent applications claiming the canceled subject matter and the claim cancellations should not be construed as abandonment or agreement with the Examiner's position in the Office Action.

Information Disclosure Statement.

Applicants note with appreciation the Examiner's thorough consideration of the references cited in the Information Disclosure Statements (Forms 1449) submitted on August 20, 2002 and on February 26, 2003.

Claim Objection.

Claim 14 was objected to because of its dependence on claim 32. Claim 14 is amended herein to depend from claim 1 thereby obviating this objection.

Obviousness-Type Double Patenting.

Claims 1-14 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting in light of claims 1-13 of copending Application No: 10/456,943.

Applicants note this is a **provisional** obviousness-type double patenting rejection because the allegedly conflicting claims have not yet been patented. Accordingly, no action is necessary at this time.

35 U.S.C. §112, First Paragraph.

Claims 1-14 were rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. In particular, the Examiner indicated that for the purposes of examination the "plurality of glass or quartz spotting capillaries" has been interpreted as having virtually any internal diameter, external diameter, load volume, aperture diameter, and center

to center spacing. The Examiner further indicated that said "microarray print head" has been interpreted as encompassing an infinite number of said capillaries. Applicants traverse by amendment and argument.

Claim 1 as amended herein recites:

1. A microarray print head, said print head comprising:
a plurality of glass or quartz spotting capillary tubes disposed in a support that maintains a fixed spacing between said spotting capillaries and that permits the spotting capillary tubes to move in a direction parallel to the long axis of said capillary tubes, wherein said capillary tubes:
have an internal diameter ranging from about 20 μ m to about 100 μ m;
have an aperture ID or OD ranging from about 20 μ m to about 75 μ m;
have an outside diameter ranging from about 0.4 mm to about 1 mm;
have a center-to-center spacing ranging from about 1 mm to about 10 mm;
have a load volume ranging from about 0.05 μ L to about 1 μ L; and
range in number from about 2 to 256
wherein said capillary tubes are in fluid communication with a manifold..

The claim thus expressly recites ranges for internal diameter, aperture, outside diameter, center to center spacing, load volume, and number of capillaries. Moreover these ranges are fully supported by the specification. One of ordinary skill would readily appreciate that the Applicants were "in possession" of the claimed invention. Accordingly the rejection of claims 1-14 under 35 U.S.C. §112, first paragraph, should be withdrawn.

35 U.S.C. §103(a).

Claims 1-14 were rejected under 35 U.S.C. §103(a) as allegedly obvious in light of Schermer *et al.* (U.S. Patent 6,447,723 B1), in view of Brown *et al.* (U.S. Patent 5,807,522) and Balch (U.S. Patent 6,083,763). According to the Examiner Schermer *et al.* discloses "microarray spotting systems" but does not teach the use of capillaries. Brown *et al.* allegedly teaches the fabrication of microarrays through the use of a capillary dispenser, while Balch allegedly teaches the use of an array of capillaries for dispensing reagents to form an array of reaction sites. Applicants traverse.

A *prima facie* case of obviousness requires that the combination of the cited art, taken with general knowledge in the field, must provide **all of the elements** of the claimed invention. When a rejection depends on a combination of prior art references, there must be some teaching, suggestion,

or **motivation** to combine the references. *In re Geiger*, 815 2 USPQ2d 1276, 1278 (Fed. Cir. 1987). Moreover, to support an obviousness rejection, the cited references must additionally provide a reasonable expectation of success. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991), citing *In re Dow Chemical Co.*, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988).

In the instant case, the combination of the cited references fails to provide all of the elements of the claimed invention. Moreover, the cited references teach away from the presently claimed invention.

Claim 1, as amended herein recites

1. A microarray print head, said print head comprising:
a plurality of **glass or quartz spotting capillary tubes** disposed in a support that maintains a fixed spacing between said spotting capillaries and that permits the spotting capillary tubes to move in a direction parallel to the long axis of said capillary tubes, wherein said capillary tubes:
have an internal diameter ranging from about 20 μm to about 100 μm ;
have an aperture ID or OD ranging from about 20 μm to about 75 μm ;
have an outside diameter ranging from about 0.4 mm to about 1 mm;
have a center-to-center spacing ranging from about 1 mm to about 10 mm;
have a load volume ranging from about 0.05 μL to about 1 μL ; and
range in number from about 2 to 256;
wherein said capillary tubes are in fluid communication with a manifold.

It was a surprising discovery that glass or quartz capillary tubes could be used in an array print head of the present invention to provide precise array spot deposition and longer useful lifetimes. Moreover, because the capillary tubes used in printheads of the present invention are loaded from the printing tip, rather than the read, the capillaries are relatively short and do not substantially flex thereby improving array precision and minimizing reagent usage.

The "front loading" feature of the presently claimed printhead is reflected in the feature: "wherein said capillary tubes are in fluid communication with a manifold" and is illustrated in Figure 8.

The combination of cited references fails to provide a microarray print head comprising "... a plurality of **glass or quartz spotting capillary tubes** ..." that are **"in fluid communication with a manifold"** as recited in claim 1.

As recognized by the Examiner, Schermer *et al.* does not teach the use of capillaries (see, e.g., Office Action, page 6, paragraph 12) or a common manifold. This defect is not remedied by Brown *et al.*

To the contrary, Brown *et al.* discloses a microarray printing device comprising a "tweezers like" elongate open capillary channel" not a capillary tube as recited in the presently pending claims. Thus, for example Brown *et al.* expressly state:

FIG. 1 illustrates, in a partially schematic view, a reagent-dispensing device 10 useful in practicing the method. The device generally includes a reagent dispenser 12 having an elongate open capillary channel 14 adapted to hold a quantity of the reagent solution, such as indicated at 16, as will be described below. The capillary channel is formed by a pair of spaced-apart, coextensive, elongate members 12a, 12b which are tapered toward one another and converge at a tip or tip region 18 at the lower end of the channel. More generally, the open channel is formed by at least two elongate, spaced-apart members adapted to hold a quantity of reagent solutions and having a tip region at which aqueous solution in the channel forms a meniscus, such as the concave meniscus illustrated at 20 in FIG. 2A. The advantages of the open channel construction of the dispenser are discussed below. [emphasis added] (col. 7, lines 1-16)

Brown *et al.* goes on to describe the advantages of an "open channel" as compared to a closed channel:

From the foregoing, it will be appreciated that the tweezers-like, open-capillary dispenser tip provides the advantages that (i) the open channel of the tip facilitates rapid, efficient washing and drying before reloading the tip with a new reagent, (ii) passive capillary action can load the sample directly from a standard microwell plate while retaining sufficient sample in the open capillary reservoir for the printing of numerous arrays, (iii) open capillaries are less prone to clogging than closed capillaries, and (iv) open capillaries do not require a perfectly faced bottom surface for fluid delivery. [emphasis added] (col. 9, lines 19-29)

Brown *et al.* thus expressly teaches away from the use of closed channel "tubes" as recited in the presently pending claims.

Moreover, because the tips are loaded by passive capillary action (when dipped into a reagent reservoir) and because the tips are open and not tubes Brown *et al.* offers no teaching or suggestion of capillary tubes in fluid communication with a manifold.

Balch also teaches away from the presently claimed invention. Balch teaches the use of long flexible fused silica capillaries that are loaded from the rear (*see, e.g.*, Figure 4). Thus, the rear end of each capillary is disposed in a reservoir:

An important feature of the capillary bundle printer is the manner in which it interfaces to the printing solution storage vessel. The capillary bundles have a printing (distal) end and a storage vessel end. The printing solution is held in a sealed container **that positions every capillary in the printing bundle via a manifold so that each capillary dips into a specific well (supply chamber) of a microtiter plate, one capillary per well.** Current multi-well microtiter plates are available with 96, 384, or 1536 wells, and can contain up to 96, 384, or 1536 individual probe solutions, respectively. For microarrays containing more probe elements, multiple printing solution reservoirs or storage vessels can be interfaced to a single print head, as illustrated in FIG. 4a. This design concept eliminates the geometry problems associated with load and dispense systems. The flexible fused silica capillaries can be gathered together with the array templates or sleeves to create a print head with capillaries spaced as close as 200 μm center to center. [emphasis added] (col. 14, lines 21-39).

As illustrated in Figure 4, **the capillaries disclosed by Balch are not in fluid communication with the manifold.** To the contrary the manifold described by Balch merely acts to position the capillaries and align them with their respective reservoirs.

In contrast, the capillaries in the presently claimed print head open into (are in fluid communication with) a common manifold (*see, e.g.*, Figure 8). Because the "back end" of the capillaries in the presently claimed printhead open into a common manifold, reagents must be loaded through the "front end" (printing tip). Balch clearly leads one of skill away from such an embodiment.

The combination of Schermer *et al.*, Brown *et al.*, and Balch thus fails to teach or suggest the presently claimed invention and actually leads one of skill away from a print head comprising "... glass or quartz spotting capillary tubes. . . " where the "capillary tubes are in fluid communication with a manifold". Accordingly the rejection of claims 1-12, and 14 under 35 U.S.C. §103(a) in light of these references should be withdrawn.

Applicants further note that Balch also expressly teaches away from the features of claim 11. Claim 11, presently recites:

11. The print head of claim 1, wherein said print head comprises a spring attached to a spotting capillary tube where, in the absence of a force against the printing tip of said spotting capillary tube said spring returns said spotting capillary tube to a rest position. [emphasis added]

In contrast, Balch teaches

The printing system can print high density probe arrays covering the bottom surface of microplate wells. To accomplish this, the printing system must be able to maintain a precise printing pattern and accommodate irregular surfaces. Rigid tubes could be used to maintain a precise pattern, however, they cannot readily accommodate irregular surfaces. Flexible tubes will print on uneven surfaces but will not maintain a precise printing pattern. The rigid sleeves, which extend below the aluminum holder assembly approximately 2 cm, support the flexible 190 μ m OD fused silica capillary tubing and provide the structural rigidity necessary to maintain a precise grid pattern over this distance. The sleeves also allow the 190 μ m tubing to travel smoothly in the Z axis during printing. This ability coupled with the flexibility of the small OD capillary tubing allows for successful printing on surfaces that are not completely flat or absolutely perpendicular to the printing fixture. Since the robot arm extends 0.1 mm to 0.3 mm beyond the point where the capillary bundle contacts the surface, the capillaries flex in the deflection zone illustrated in FIG. 4 resulting in total surface contact among all capillaries in the bundle. When the printing fixture withdraws from the substrate, the capillaries straighten, returning to their original positions. [emphasis added] (col. 13, lines 1-22)

Thus, Balch teaches the use of flexible capillaries that flex in a "deflection zone" to accommodate irregularities in the printing surface. The capillaries then return to their original position by passive "straightening" of the capillary. There is no provision for a spring or other means to return the capillary to its original position as recited in claim 11. Moreover, Balch teaches the importance of such a flexion zone and thereby leads one of skill away from the embodiment claimed in presently pending claim 11. Accordingly, for these reasons as well as the reasons given above, the combination of Schermer *et al.*, Brown *et al.*, and Balch fails to teach or suggest the invention of claim 11 and the rejection under 35 U.S.C. §103(a) in light of these references should be withdrawn.

In view of the foregoing, Applicants believes all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is

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respectfully requested. Should the Examiner seek to maintain the rejections, Applicants request a telephone interview with the Examiner and the Examiner's supervisor.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (510) 769-3513.

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Respectfully submitted,



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